

Timing of Rotavirus Vaccine Doses and Incidence of Severe Rotavirus Gastroenteritis among  
Vaccinated Infants in Low- and Middle-Income Countries

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Supplemental File

### *Additional Information on Methods*

Infants contributed person-time to each schedule for each aspect of timing from 12 weeks of age until the earliest of any of the following instances occurred: 1) the infant was lost to follow-up, 2) the infant experienced a severe RVGE event, or 3) the timing of the infant's actual doses deviated from the predefined timing requirements allowed for that specific schedule. eTable 1 includes detailed information on inclusion and censoring from each schedule, and eTable 2 illustrates detailed examples of two hypothetical infants in each trial and the person-time contributed for each schedule for each aspect of timing.

eTable 1. Detailed description entry, follow-up and censoring for predefined schedules for each aspect of timing.

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censoring*	
First dose with 4 – 6 weeks between doses	RV5	3 – 6 wks of age	4 – 6 wks after 1 <sup>st</sup> dose	4 – 6 wks after 2 <sup>nd</sup> dose	Infants with 1 <sup>st</sup> dose at 3, 4, 5, or 6 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose	Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose
First dose with 4 – 6 weeks between doses	RV5	7 – 9 wks of age	4 – 6 wks after 1 <sup>st</sup> dose	4 – 6 wks after 2 <sup>nd</sup> dose	Infants with 1 <sup>st</sup> dose at 7, 8, or 9 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose	Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose
First dose with 4 – 6 weeks between doses	RV5	10 – 12 wks of age	4 – 6 wks after 1 <sup>st</sup> dose	4 – 6 wks after 2 <sup>nd</sup> dose	Infants with 1 <sup>st</sup> dose at 10, 11, or 12 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose	Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose
First dose with 4 – 6 weeks between doses	RV1	10 – 12 wks of age	4 – 6 wks after 1 <sup>st</sup> dose	NA	Infants with 1 <sup>st</sup> dose at 10, 11, or 12 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 1 <sup>st</sup> dose
First dose with 4 – 6 weeks between doses	RV1	13 – 16 wks of age	4 – 6 wks after 1 <sup>st</sup> dose	NA	Infants missing first RV1 or with 1 <sup>st</sup> dose > 12 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
					No 1 <sup>st</sup> dose by 16 wks of age	16 wks of age
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose	6 wks after 1 <sup>st</sup> dose

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censoring*								
First dose	RV5	< 6 wks of age	≤ 10 wks after 1 <sup>st</sup> dose	≤ 10 wks after 2 <sup>nd</sup> dose	<div>Infants with 1<sup>st</sup> dose at &lt; 6 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr><tr><td>No 3<sup>rd</sup> dose by 10 wks after 2<sup>nd</sup> dose</td><td>10 wks after 2<sup>nd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose	No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose
Reason for Censoring	Time of Censoring												
Lost to follow-up/dropout	Time of dropout												
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No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose												
First dose	RV5	≥ 6 wks of age	≤ 10 wks after 1 <sup>st</sup> dose	≤ 10 wks after 2 <sup>nd</sup> dose	<div>Infants with 1<sup>st</sup> dose at ≥ 6 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr><tr><td>No 3<sup>rd</sup> dose by 10 wks after 2<sup>nd</sup> dose</td><td>10 wks after 2<sup>nd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose	No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose
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No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose												
First dose	RV5	< 10 wks of age	≤ 10 wks after 1 <sup>st</sup> dose	≤ 10 wks after 2 <sup>nd</sup> dose	<div>Infants with 1<sup>st</sup> dose at &lt; 10 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr><tr><td>No 3<sup>rd</sup> dose by 10 wks after 2<sup>nd</sup> dose</td><td>10 wks after 2<sup>nd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose	No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose
Reason for Censoring	Time of Censoring												
Lost to follow-up/dropout	Time of dropout												
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No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose												
First dose	RV5	≥ 10 wks of age	≤ 10 wks after 1 <sup>st</sup> dose	≤ 10 wks after 2 <sup>nd</sup> dose	<div>Infants with 1<sup>st</sup> dose at ≥ 10 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr><tr><td>No 3<sup>rd</sup> dose by 10 wks after 2<sup>nd</sup> dose</td><td>10 wks after 2<sup>nd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose	No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose
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No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose												

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censoring*										
Last dose	RV5	≤ 7 wks of age	≤ 11	≤ 15	<div>Infants with 1<sup>st</sup> dose at ≤ 7 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 11 wks of age</td><td>11 wks of age</td></tr><tr><td>No 3<sup>rd</sup> dose by 15 wks of age</td><td>15 wks of age</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 11 wks of age	11 wks of age	No 3 <sup>rd</sup> dose by 15 wks of age	15 wks of age		
Reason for Censoring	Time of Censoring														
Lost to follow-up/dropout	Time of dropout														
No 2 <sup>nd</sup> dose by 11 wks of age	11 wks of age														
No 3 <sup>rd</sup> dose by 15 wks of age	15 wks of age														
Last dose	RV5	≤ 12 wks of age	≤ 10 wks after 1 <sup>st</sup> dose	> 15 & ≤ 10 wks after 2 <sup>nd</sup> dose	<div>All infants begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr><tr><td>Receipt of 3<sup>rd</sup> dose ≤ 15 wks of age</td><td>Time of 3<sup>rd</sup> dose</td></tr><tr><td>No 3<sup>rd</sup> dose by 10 wks after 2<sup>nd</sup> dose</td><td>10 wks after 2<sup>nd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose	Receipt of 3 <sup>rd</sup> dose ≤ 15 wks of age	Time of 3 <sup>rd</sup> dose	No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose
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Receipt of 3 <sup>rd</sup> dose ≤ 15 wks of age	Time of 3 <sup>rd</sup> dose														
No 3 <sup>rd</sup> dose by 10 wks after 2 <sup>nd</sup> dose	10 wks after 2 <sup>nd</sup> dose														
Last dose	RV1	≤ 11 wks of age	≤ 15 wks of age	NA	<div>Infants with 1<sup>st</sup> dose at ≤ 11 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 2<sup>nd</sup> dose by 15 wks of age</td><td>15 wks of age</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 2 <sup>nd</sup> dose by 15 wks of age	15 wks of age				
Reason for Censoring	Time of Censoring														
Lost to follow-up/dropout	Time of dropout														
No 2 <sup>nd</sup> dose by 15 wks of age	15 wks of age														
Last dose	RV1	≤ 16 wks of age	> 15 wks of age & ≤ 10 wks after 2 <sup>nd</sup> dose	NA	<div>All infants begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>No 1<sup>st</sup> dose by 16 wks of age</td><td>16 wks of age</td></tr><tr><td>Receipt of 2<sup>nd</sup> dose ≤ 15 wks of age</td><td>Time of 2<sup>nd</sup> dose</td></tr><tr><td>No 2<sup>nd</sup> dose by 10 wks after 1<sup>st</sup> dose</td><td>10 wks after 1<sup>st</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	No 1 <sup>st</sup> dose by 16 wks of age	16 wks of age	Receipt of 2 <sup>nd</sup> dose ≤ 15 wks of age	Time of 2 <sup>nd</sup> dose	No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose
Reason for Censoring	Time of Censoring														
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No 1 <sup>st</sup> dose by 16 wks of age	16 wks of age														
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No 2 <sup>nd</sup> dose by 10 wks after 1 <sup>st</sup> dose	10 wks after 1 <sup>st</sup> dose														

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censoring*
Interval between doses	RV5	≤ 12 wks of age	4 wks after 1 <sup>st</sup> dose	4 wks after 2 <sup>nd</sup> dose	All infants begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:
					Reason for Censoring
					Time of Censoring
					Lost to follow-up/dropout
					Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose
Interval between doses	RV5	≤ 12 wks of age	5 wks after 1 <sup>st</sup> dose	4 wks after 2 <sup>nd</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 4 wks after 1 <sup>st</sup> dose
					4 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose
					Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 4 wks after 2 <sup>nd</sup> dose
Interval between doses	RV5	≤ 12 wks of age	5 wks after 1 <sup>st</sup> dose	5 wks after 2 <sup>nd</sup> dose	4 wks after 2 <sup>nd</sup> dose
					Reason for Censoring
					Time of Censoring
					Lost to follow-up/dropout
					Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose
Interval between doses	RV5	≤ 12 wks of age	5 wks after 1 <sup>st</sup> dose	5 wks after 2 <sup>nd</sup> dose	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 5 wks after 1 <sup>st</sup> dose
					5 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose
					Time of 3 <sup>rd</sup> dose
					Receipt of 3 <sup>rd</sup> dose at 4 wks after 2 <sup>nd</sup> dose when 2 <sup>nd</sup> dose received 4 wks after 1 <sup>st</sup> dose
Interval between doses	RV5	≤ 12 wks of age	6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose	Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose at 4 wks after 2 <sup>nd</sup> dose when 2 <sup>nd</sup> dose received 4 or 5 wks after 1 <sup>st</sup> dose
					Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 5 wks after 2 <sup>nd</sup> dose
					5 wks after 2 <sup>nd</sup> dose
					Reason for Censoring
Interval between doses	RV5	≤ 12 wks of age	6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose	Time of Censoring
					Lost to follow-up/dropout
					Time of dropout
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose
					Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose
Interval between doses	RV5	≤ 12 wks of age	6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose	6 wks after 1 <sup>st</sup> dose
					Receipt of 3 <sup>rd</sup> dose < 4 wks after 2 <sup>nd</sup> dose
					Time of 3 <sup>rd</sup> dose
					Receipt of 3 <sup>rd</sup> dose at 4 wks after 2 <sup>nd</sup> dose when 2 <sup>nd</sup> dose received 4 or 5 wks after 1 <sup>st</sup> dose
					Time of 3 <sup>rd</sup> dose
					Receipt of 3 <sup>rd</sup> dose at 5 wks after 2 <sup>nd</sup> dose when 2 <sup>nd</sup> dose received 4 or 5 wks after 1 <sup>st</sup> dose
Interval between doses	RV5	≤ 12 wks of age	6 wks after 1 <sup>st</sup> dose	6 wks after 2 <sup>nd</sup> dose	Time of 3 <sup>rd</sup> dose
					No 3 <sup>rd</sup> dose by 6 wks after 2 <sup>nd</sup> dose
					6 wks after 2 <sup>nd</sup> dose
Interval between doses	RV1	≤ 16 wks of age	4 wks after 1 <sup>st</sup> dose	NA	All infants begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:
					Reason for Censoring
					Time of Censoring
					Lost to follow-up/dropout
					Time of dropout
					No 1 <sup>st</sup> dose by 16 wks of age
Interval between doses	RV1	≤ 16 wks of age	5 wks after 1 <sup>st</sup> dose	NA	16 wks of age
					Receipt of 2 <sup>nd</sup> dose < 4 wks after 1 <sup>st</sup> dose
					Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 4 wks after 1 <sup>st</sup> dose
					4 wks after 1 <sup>st</sup> dose
					Reason for Censoring
Interval between doses	RV1	≤ 16 wks of age	6 wks after 1 <sup>st</sup> dose	NA	Time of Censoring
					Lost to follow-up/dropout
					Time of dropout
					No 1 <sup>st</sup> dose by 16 wks of age
					16 wks of age
					Receipt of 2 <sup>nd</sup> dose < 5 wks after 1 <sup>st</sup> dose
Interval between doses	RV1	≤ 16 wks of age	6 wks after 1 <sup>st</sup> dose	NA	Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 5 wks after 1 <sup>st</sup> dose
					5 wks after 1 <sup>st</sup> dose
					Reason for Censoring
					Time of Censoring
					Lost to follow-up/dropout
Interval between doses	RV1	≤ 16 wks of age	6 wks after 1 <sup>st</sup> dose	NA	Time of dropout
					No 1 <sup>st</sup> dose by 16 wks of age
					16 wks of age
					Receipt of 2 <sup>nd</sup> dose < 6 wks after 1 <sup>st</sup> dose
					Time of 2 <sup>nd</sup> dose
					No 2 <sup>nd</sup> dose by 6 wks after 1 <sup>st</sup> dose
					6 wks after 1 <sup>st</sup> dose

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censoring*														
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	< 10 wks of age	<div>All Infants with 1<sup>st</sup> dose at &lt; 10 wks of age begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>Receipt of 2<sup>nd</sup> dose <math>\geq</math> 10 wks of age</td><td>Time of 2<sup>nd</sup> dose</td></tr><tr><td>Receipt of 3<sup>rd</sup> dose <math>\geq</math> 10 wks of age</td><td>Time of 3<sup>rd</sup> dose</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	Receipt of 2 <sup>nd</sup> dose $\geq$ 10 wks of age	Time of 2 <sup>nd</sup> dose	Receipt of 3 <sup>rd</sup> dose $\geq$ 10 wks of age	Time of 3 <sup>rd</sup> dose						
Reason for Censoring	Time of Censoring																		
Lost to follow-up/dropout	Time of dropout																		
Receipt of 2 <sup>nd</sup> dose $\geq$ 10 wks of age	Time of 2 <sup>nd</sup> dose																		
Receipt of 3 <sup>rd</sup> dose $\geq$ 10 wks of age	Time of 3 <sup>rd</sup> dose																		
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	No 3 <sup>rd</sup> dose															
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	No 2 <sup>nd</sup> dose	No 3 <sup>rd</sup> dose															
Number of doses $\geq$ 10 weeks of age	RV5	$\geq$ 10 wks of age	No 2 <sup>nd</sup> dose	No 3 <sup>rd</sup> dose	<div>All Infants begin in this group and continue follow-up until severe RVGE, end of study, or censoring. Infants are censored at the earliest occurrence of any of the following:</div> <table><tr><th>Reason for Censoring</th><th>Time of Censoring</th></tr><tr><td>Lost to follow-up/dropout</td><td>Time of dropout</td></tr><tr><td>Receipt of 3<sup>rd</sup> dose &lt; 10 wks of age</td><td>Time of 3<sup>rd</sup> dose</td></tr><tr><td>Receipt of 2<sup>nd</sup> dose when 1<sup>st</sup> dose received <math>\geq</math> 10 wks of age</td><td>Time of 2<sup>nd</sup> dose</td></tr><tr><td>Receipt of 3<sup>rd</sup> dose when 2<sup>nd</sup> dose received <math>\geq</math> 10 wks of age</td><td>Time of 3<sup>rd</sup> dose</td></tr><tr><td>No 2<sup>nd</sup> dose by 32 wks of age when 1<sup>st</sup> dose received &lt; 10 wks of age</td><td>32 wks of age</td></tr><tr><td>No 3<sup>rd</sup> dose by 32 wks of age when 2<sup>nd</sup> dose received &lt; 10 wks of age</td><td>32 wks of age</td></tr></table>	Reason for Censoring	Time of Censoring	Lost to follow-up/dropout	Time of dropout	Receipt of 3 <sup>rd</sup> dose < 10 wks of age	Time of 3 <sup>rd</sup> dose	Receipt of 2 <sup>nd</sup> dose when 1 <sup>st</sup> dose received $\geq$ 10 wks of age	Time of 2 <sup>nd</sup> dose	Receipt of 3 <sup>rd</sup> dose when 2 <sup>nd</sup> dose received $\geq$ 10 wks of age	Time of 3 <sup>rd</sup> dose	No 2 <sup>nd</sup> dose by 32 wks of age when 1 <sup>st</sup> dose received < 10 wks of age	32 wks of age	No 3 <sup>rd</sup> dose by 32 wks of age when 2 <sup>nd</sup> dose received < 10 wks of age	32 wks of age
Reason for Censoring	Time of Censoring																		
Lost to follow-up/dropout	Time of dropout																		
Receipt of 3 <sup>rd</sup> dose < 10 wks of age	Time of 3 <sup>rd</sup> dose																		
Receipt of 2 <sup>nd</sup> dose when 1 <sup>st</sup> dose received $\geq$ 10 wks of age	Time of 2 <sup>nd</sup> dose																		
Receipt of 3 <sup>rd</sup> dose when 2 <sup>nd</sup> dose received $\geq$ 10 wks of age	Time of 3 <sup>rd</sup> dose																		
No 2 <sup>nd</sup> dose by 32 wks of age when 1 <sup>st</sup> dose received < 10 wks of age	32 wks of age																		
No 3 <sup>rd</sup> dose by 32 wks of age when 2 <sup>nd</sup> dose received < 10 wks of age	32 wks of age																		
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	$\geq$ 10 & $\leq$ 32	No 3 <sup>rd</sup> dose															
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age															
Number of doses $\geq$ 10 weeks of age	RV5	$\geq$ 10 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age	No 3 <sup>rd</sup> dose															
Number of doses $\geq$ 10 weeks of age	RV5	< 10 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age															
Number of doses $\geq$ 10 weeks of age	RV5	$\geq$ 10 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age															
Number of doses $\geq$ 10 weeks of age	RV5	$\geq$ 10 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age	$\geq$ 10 wks of age & $\leq$ 32 wks of age															

RV1, monovalent rotavirus vaccine; RV5, pentavalent rotavirus vaccine; Wks, weeks; NA, not applicable

\*Censoring for those not receiving a first dose of vaccine is not described for the RV5 trial; all infants in the RV5 trial received at least 1 dose of vaccine, but some infants in the RV1 trial did not receive a dose of vaccine.

eTable 2. Example of entry, follow-up, and censoring for predefined schedules for each aspect of timing for two hypothetical infants receiving RV5 (infants A and B) and RV1 (infants C and D). Follow-up is indicated by gray.

Aspect of Timing	Infant	RV Type	Age at Dose (weeks)			Predefined Schedules	Age in weeks									
			Dose 1	Dose 2	Dose 3		12	13	14	15	16	17	18	19	20	
First dose with 4 – 6 weeks between doses	A	RV5	5	10	18	3-6 weeks with 4-6 week intervals 7-9 weeks with 4-6 week intervals 10-12 weeks with 4-6 week intervals										
	B	RV5	10	16	20	3-6 weeks with 4-6 week intervals 7-9 weeks with 4-6 week intervals 10-12 weeks with 4-6 week intervals										
	C	RV1	10	15		10-12 weeks with 4-6 week intervals 13-16 weeks with 4-6 week intervals										
	D	RV1	14	18		10-12 weeks with 4-6 week intervals 13-16 weeks with 4-6 week intervals										
First dose	A	RV5	5	10	18	1 <sup>st</sup> dose < 6 weeks 1 <sup>st</sup> dose ≥ 6 weeks										
	B	RV5	10	16	20	1 <sup>st</sup> dose < 6 weeks 1 <sup>st</sup> dose ≥ 6 weeks										
Last dose	A	RV5	5	10	18	3 <sup>rd</sup> dose ≤ 15 weeks 3 <sup>rd</sup> dose > 15 weeks										
	B	RV5	10	16	20	3 <sup>rd</sup> dose ≤ 15 weeks 3 <sup>rd</sup> dose > 15 weeks										
	C	RV1	10	15		2 <sup>nd</sup> dose ≤ 15 weeks 2 <sup>nd</sup> dose > 15 weeks										
	D	RV1	14	18		2 <sup>nd</sup> dose ≤ 15 weeks 2 <sup>nd</sup> dose > 15 weeks										
Interval between doses	A	RV5	5	10	18	Both 4 weeks ≥ 1 of 5 weeks ≥ 1 of 6 weeks										
	B	RV5	10	16	20	Both 4 weeks ≥ 1 of 5 weeks ≥ 1 of 6 weeks										
	C	RV1	10	15		4 weeks 5 weeks 6 weeks										
	D	RV1	14	18		4 weeks 5 weeks 6 weeks										
Number of doses ≥ 10 weeks of age	A	RV5	5	10	18	1 dose at ≥ 10 weeks 2 doses at ≥ 10 weeks 3 doses at ≥ 10 weeks										
	B	RV5	10	16	20	1 dose at ≥ 10 weeks 2 doses at ≥ 10 weeks 3 doses at ≥ 10 weeks										



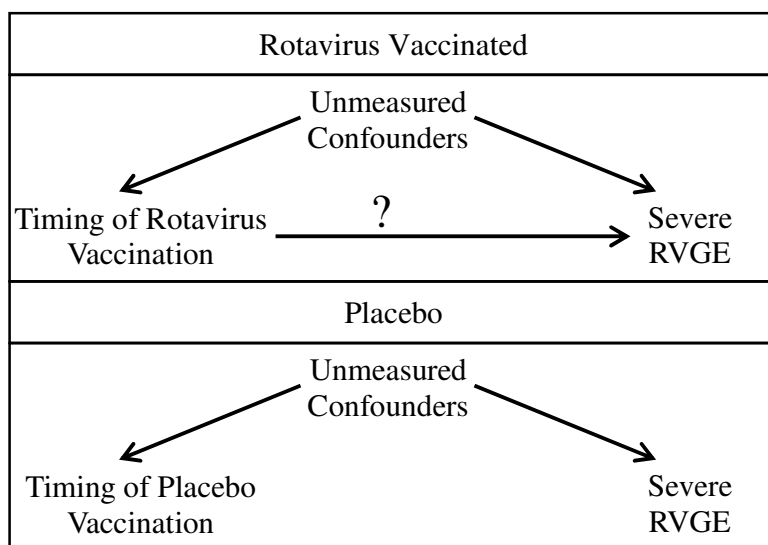
eTable 3. Number of expected severe RVGE episodes that would occur if altering vaccination schedules had no benefit.

Cohort	Expected Increase in RVGE Episodes per 1,000 Infants (95% CI)*	
	RV1	RV5
	6/10 vs. 10/14	6/10/14 vs. 8/12/16
Cohort 1 <sup>†</sup>	5 (1, 8)	2 (0, 4)
Cohort 2 <sup>‡</sup>	1 (0, 2)	0 (0, 1)

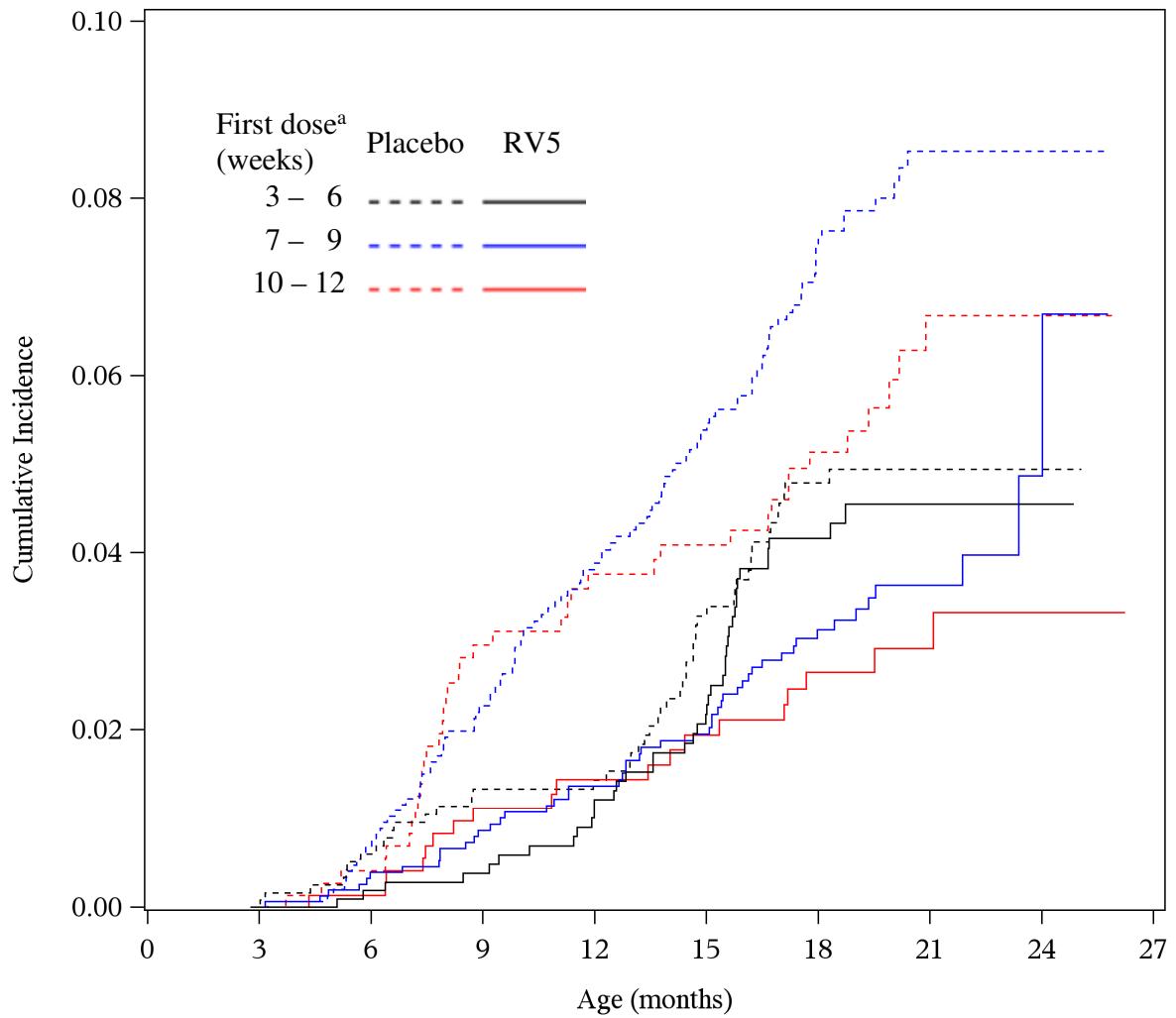
\* Estimates assume infants are fully protected at two weeks following the final dose of vaccine. Therefore, the expected increase is for the period from 12 to 16 weeks (RV1) and 16 to 18 weeks (RV5). These estimates also assume the severe RVGE episodes would be prevented had infants been vaccinated at 6/10 (RV1) or 6/10/14 (RV5) weeks and that there is no partial protection for an incomplete series for later vaccine schedules.

<sup>†</sup> Estimates for shifting RV1 or RV5 schedules using the placebo arm in RV1 Trial.

<sup>‡</sup> Estimates for shifting RV1 or RV5 schedules using the placebo arm in RV5 Trial.



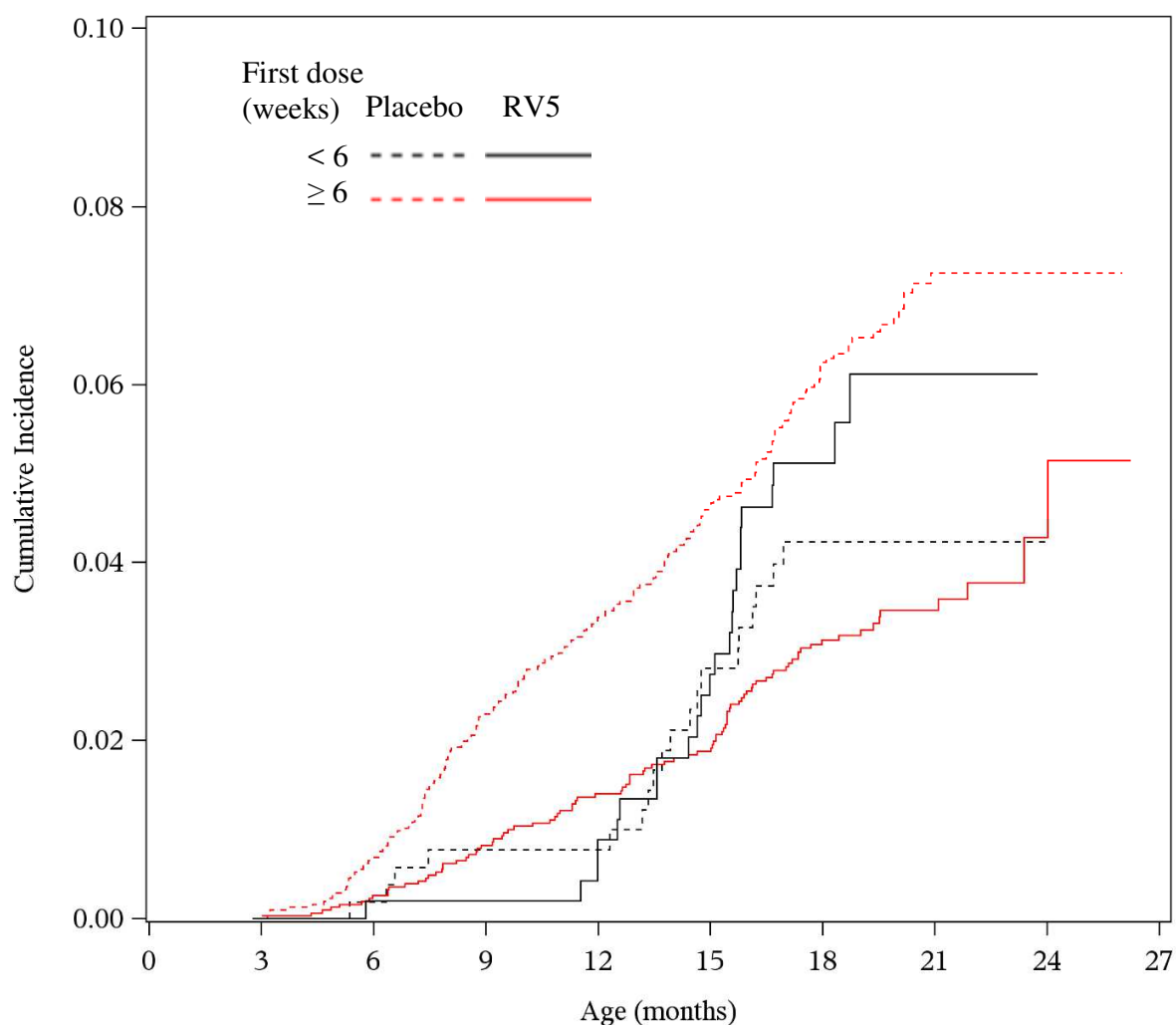
eFigure 1. Two directed acyclic graphs in the rotavirus vaccinated (top panel) and placebo (bottom panel) arms. We are interested in the effect of timing of rotavirus vaccination on incidence of severe RVGE. However, unmeasured confounders affecting both the timing of rotavirus vaccination and incidence of severe RVGE may make it appear that there is an association when one does not exist. In the placebo arm, the timing of placebo doses should not influence the incidence of severe RVGE. However, if there is an association between timing of placebo vaccination and severe RVGE, this would be due to unmeasured confounders. If we assume the same unmeasured confounders exist in both treatment arms (treatments were blinded), then we can adjust for unmeasured confounders in the rotavirus vaccinated arm by calibrating the estimates from the rotavirus vaccinated arm with the estimates from the placebo arm. This calibration would result in the removal of any effect due to confounders.



<sup>a</sup> with 4-6 weeks between doses

Vaccine Type	Age of first dose (weeks) with 4-6 weeks between doses	N				
RV5	3 – 6	1,167	1,073	943	640	7
	7 – 9	1,669	1,516	1,351	1,003	52
	10 – 12	784	720	600	527	45
Placebo	3 – 6	1,250	1,134	980	687	9
	7 – 9	1,589	1,451	1,293	948	64
	10 – 12	780	713	590	514	39

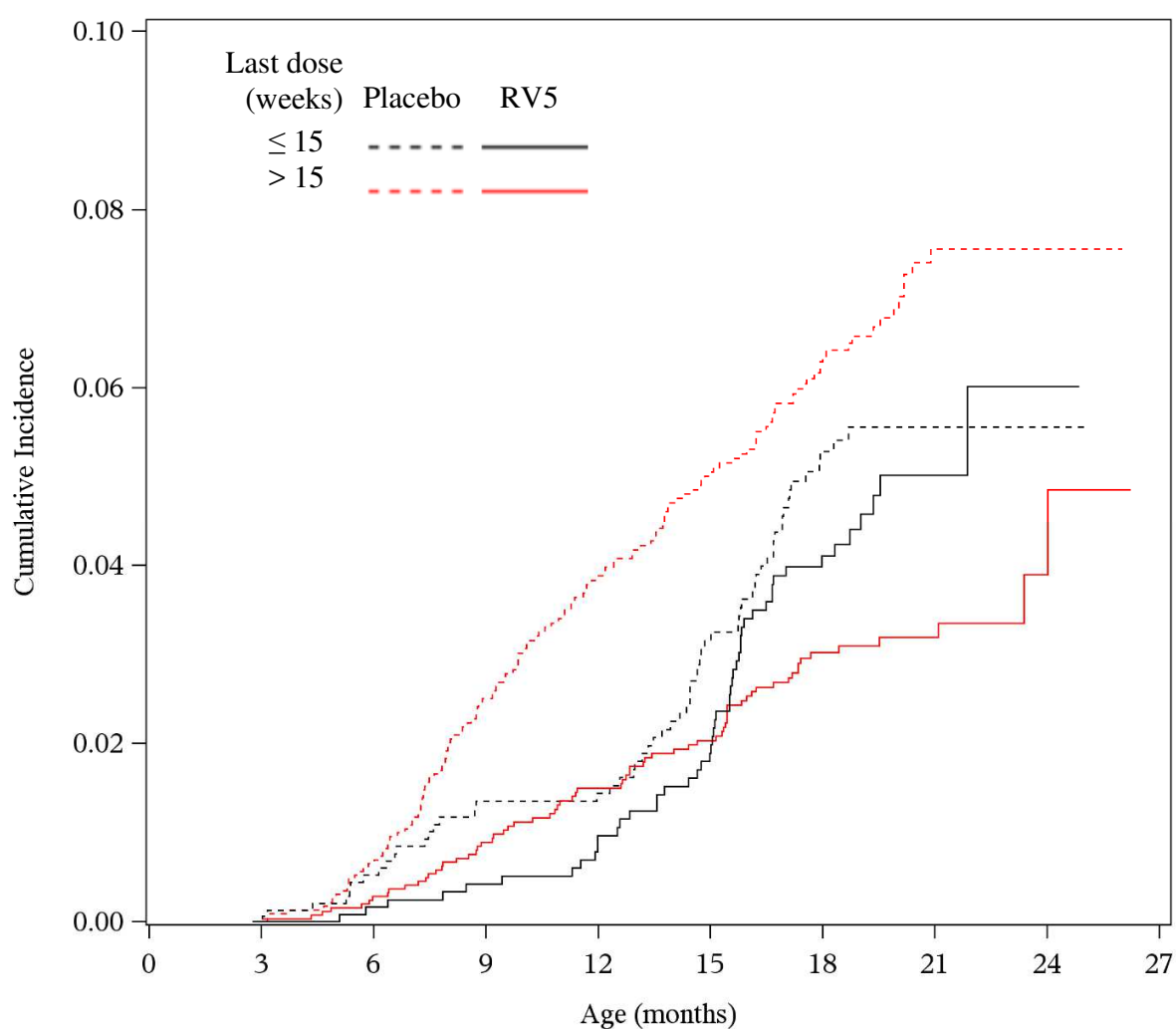
eFigure 2. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose (weeks) with 4 – 6 week intervals between subsequent doses in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for schedule is below the x-axis.



Vaccine Type	Age of first dose (weeks)	N				
		12 weeks	6 months	12 months	18 months	24 months
RV5	< 6	519	506	432	255	0
	≥ 6	3,147	3,063	2,700	2,055	109
Placebo	< 6	548	534	445	274	0
	≥ 6	3,127	3,011	2,640	1,993	114

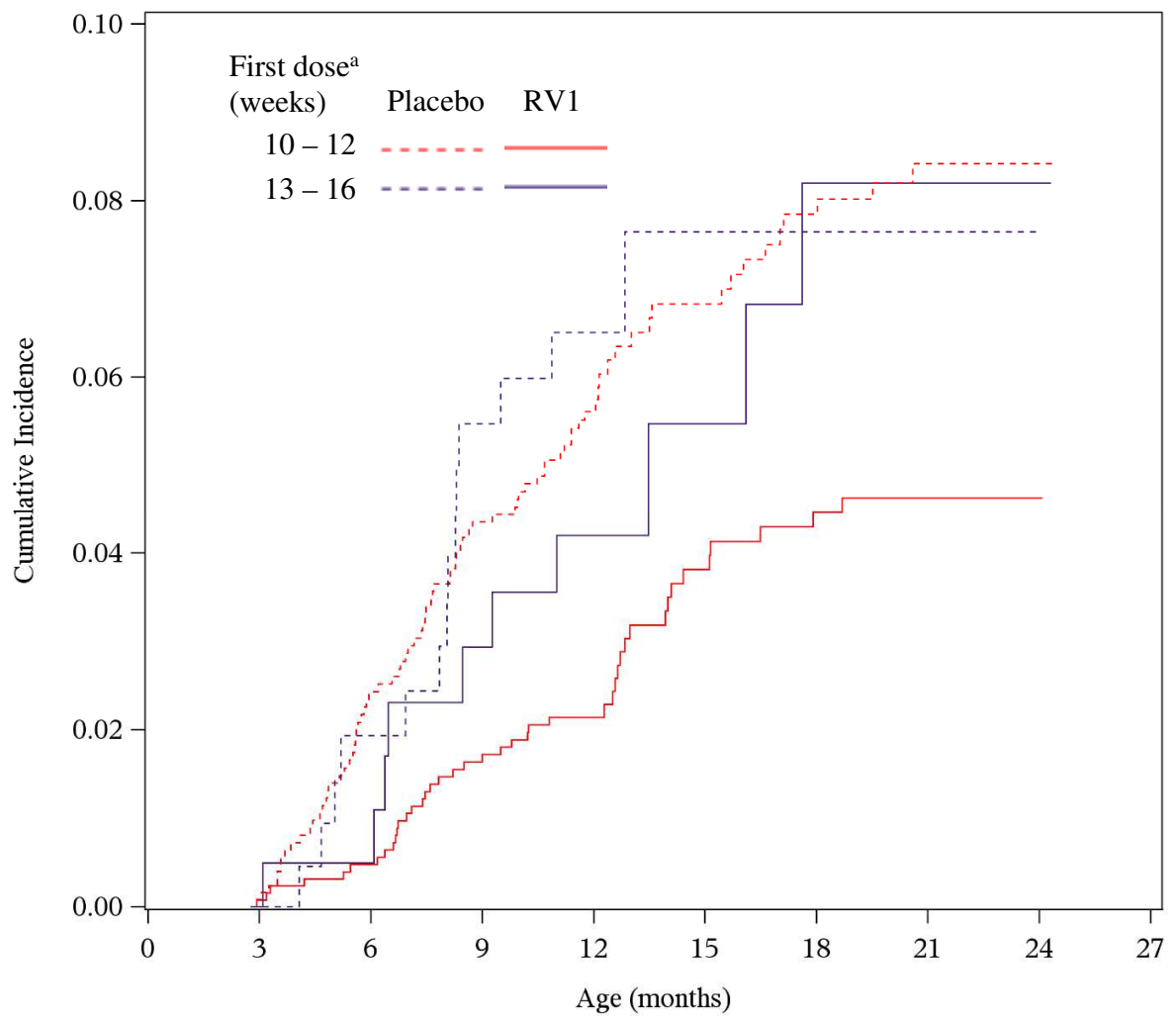
eFigure 3. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose (< 6 weeks vs. ≥ 6 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.





Vaccine Type	Age of last dose (weeks)	N				
		12 weeks	6 months	12 months	18 months	24 months
RV5	≤ 15	1,527	1,216	1,087	778	9
	> 15	3,520	2,353	2,045	1,532	100
Placebo	≤ 15	1,596	1,253	1,104	803	12
	> 15	3,534	2,292	1,981	1,464	102

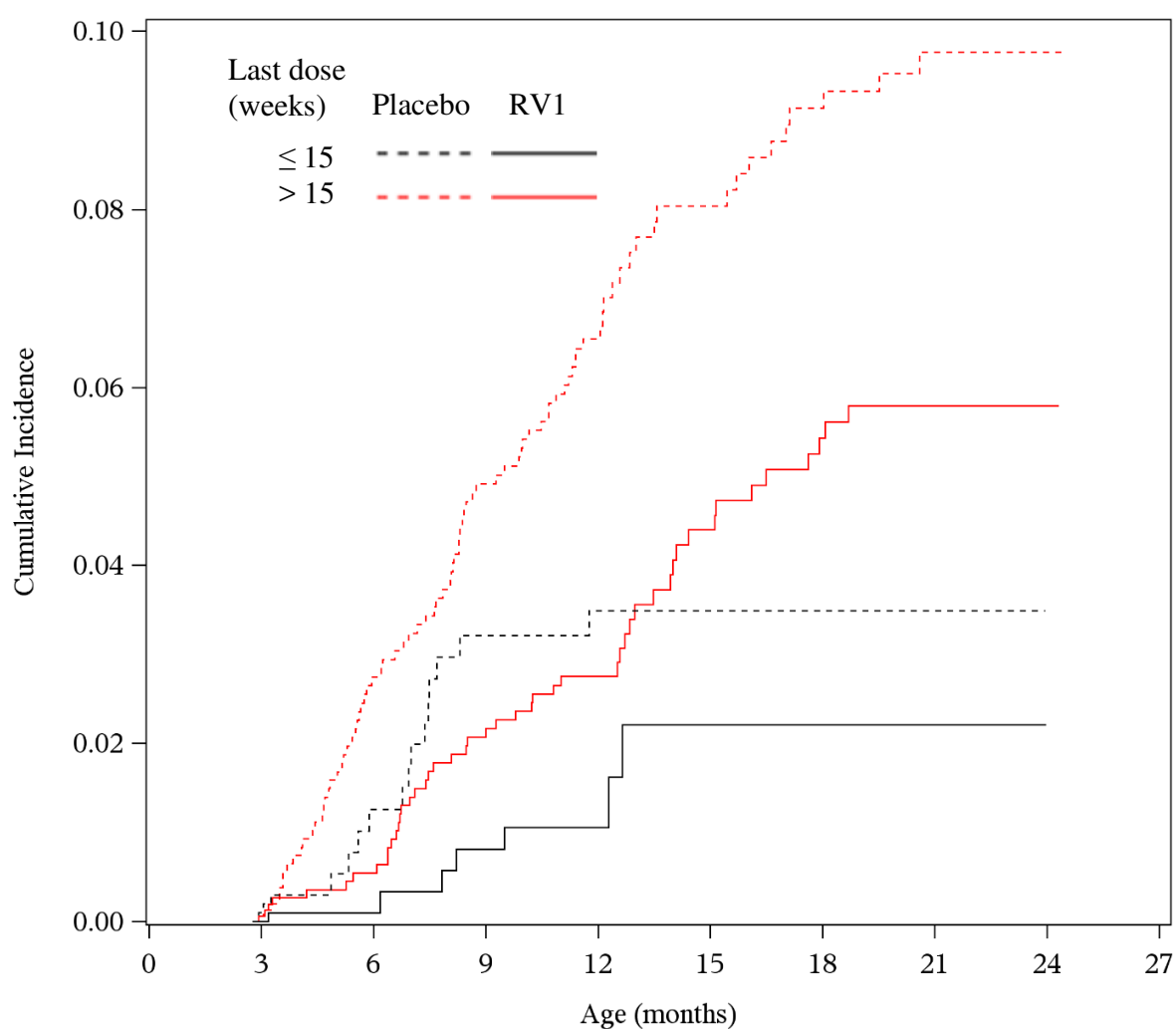
eFigure 5. Cumulative incidence of severe rotavirus gastroenteritis by age of last dose ( $\leq 15$  weeks vs.  $> 15$  weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



<sup>a</sup> with 4-6 weeks between doses

Vaccine Type	Age of first dose (weeks) with 4-6 weeks between doses	N				
		12 weeks	6 months	12 months	18 months	24 months
RV1	10 – 12	1,299	1,212	767	573	7
	13 – 16	207	166	100	67	1
Placebo	10 – 12	1,255	1,128	708	530	6
	13 – 16	253	196	107	73	1

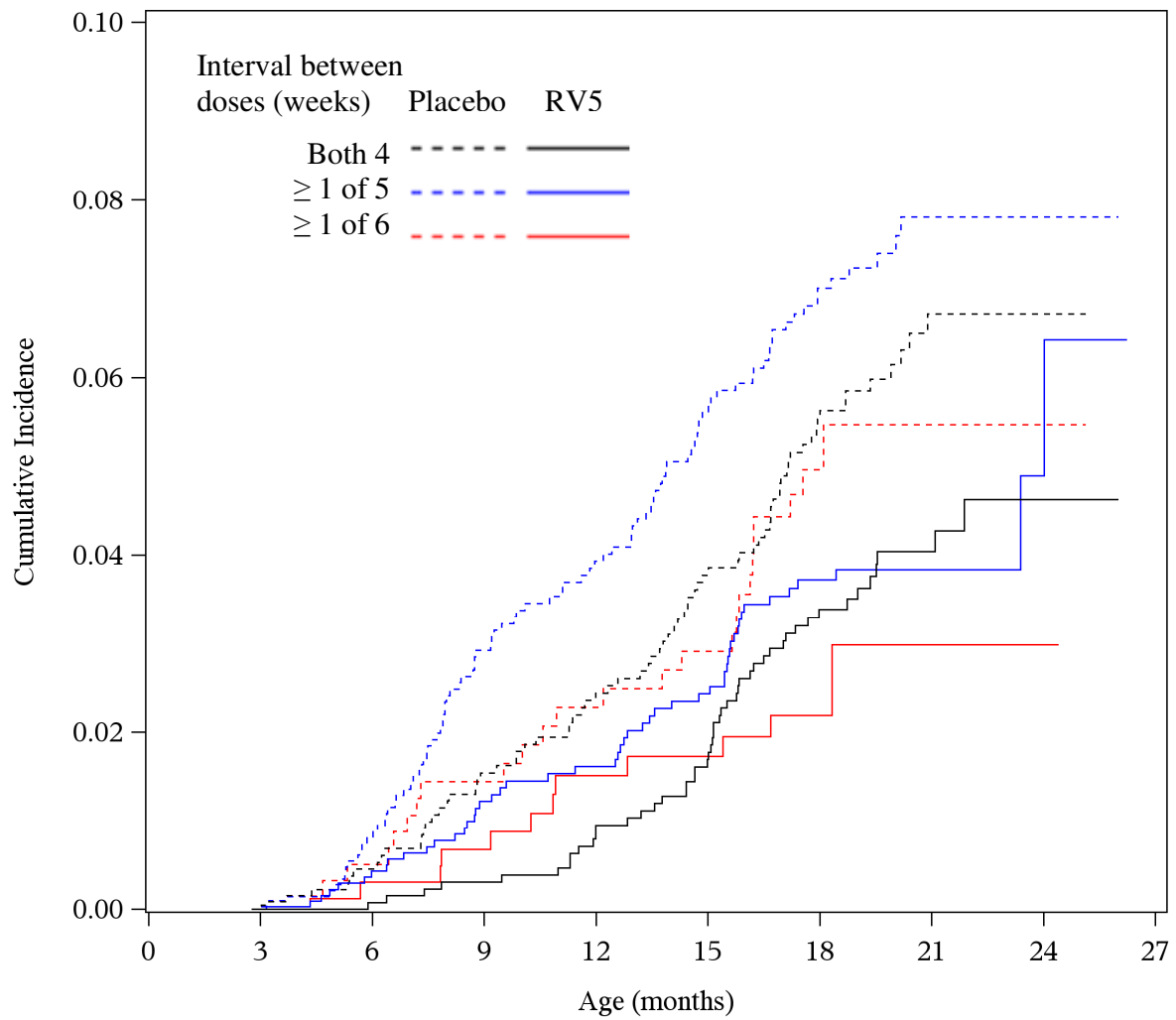
eFigure 6. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose with a 4 – 6 weeks between doses in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for schedule is below the x-axis.



Vaccine Type	Age of last dose (weeks)	N				
		12 weeks	6 months	12 months	18 months	24 months
RV5	≤ 15	1,048	420	218	149	0
	> 15	1,559	1,056	702	531	8
Placebo	≤ 15	998	408	220	152	0
	> 15	1,553	996	636	481	7

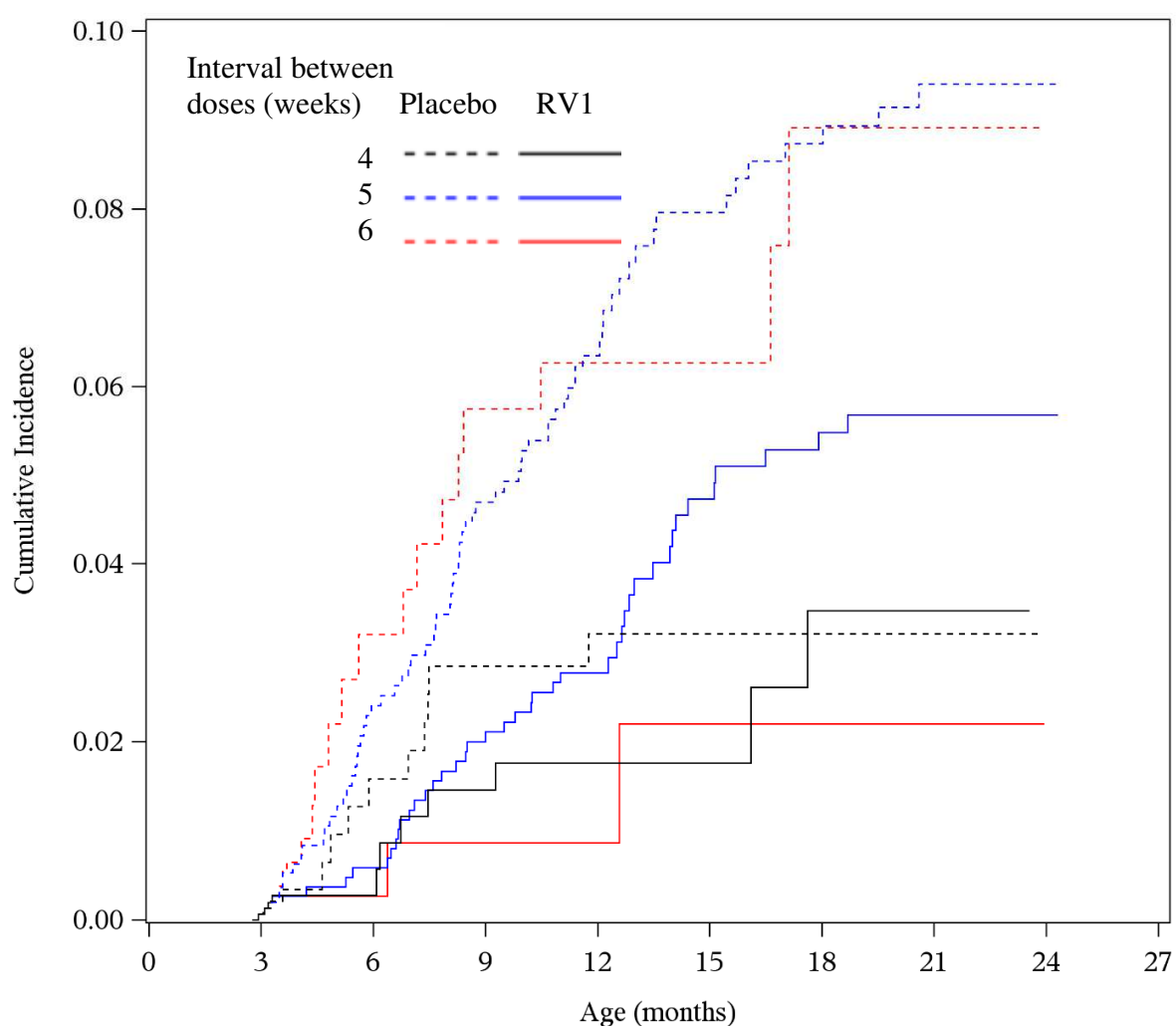
eFigure 7. Cumulative incidence of severe rotavirus gastroenteritis by age of last dose ( $\leq 15$  weeks vs.  $> 15$  weeks) in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.





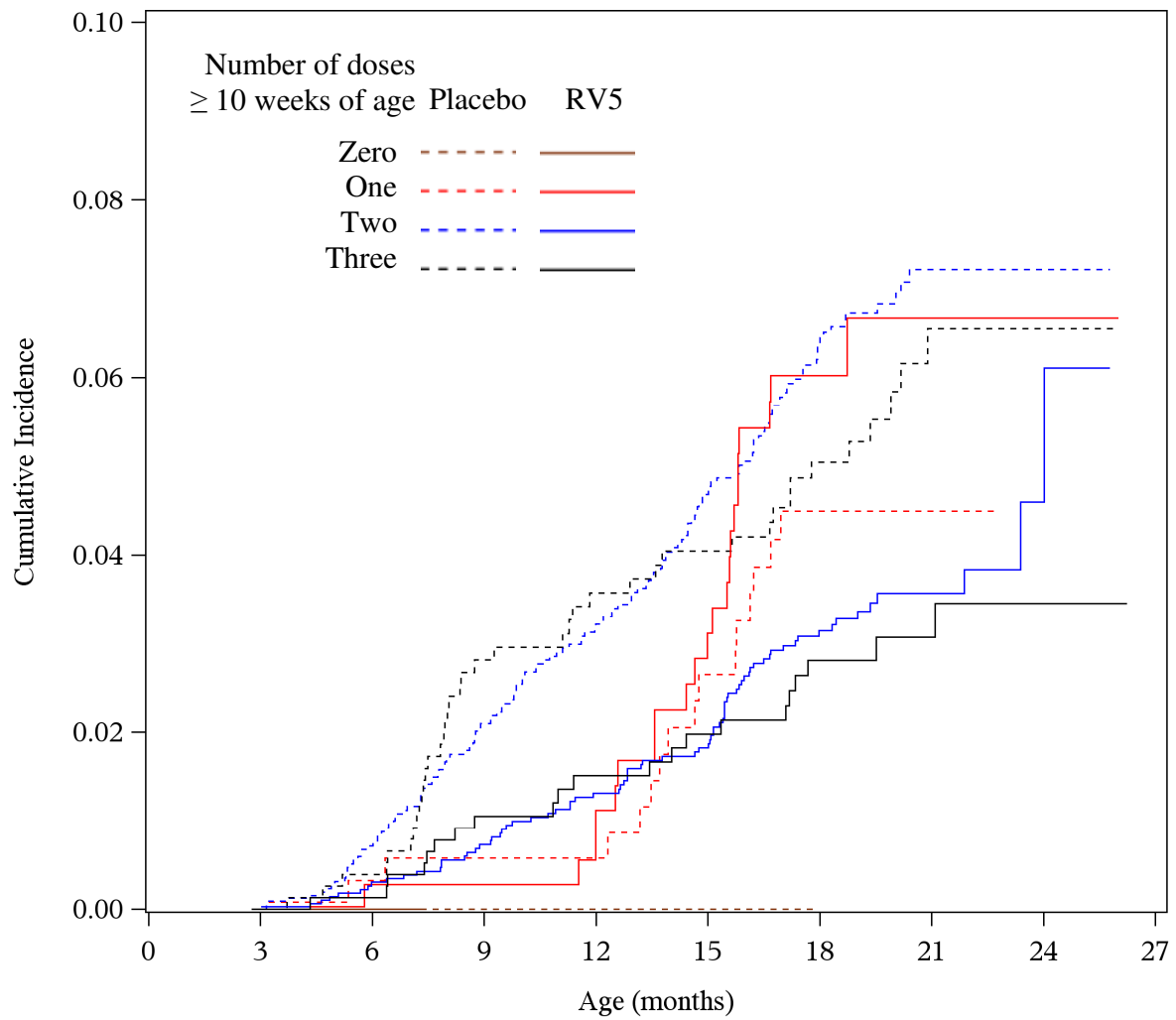
Vaccine Type	Intervals between doses (weeks)	N				
		2,589	1,310	1,219	1,003	39
RV5	Both 4	2,589	1,310	1,219	1,003	39
	≥ 1 of 5	3,345	1,453	1,215	939	62
	≥ 1 of 6	3,474	546	460	228	3
Placebo	Both 4	2,531	1,298	1,187	968	41
	≥ 1 of 5	3,343	1,464	1,211	939	64
	≥ 1 of 6	3,478	536	465	242	7

eFigure 8. Cumulative incidence of severe rotavirus gastroenteritis by length of interval between doses (both intervals 4 weeks vs.  $\geq 1$  interval of 5 weeks vs.  $\geq 1$  interval of 6 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



Vaccine Type	Interval between doses (weeks)	N				
		12 weeks	6 months	12 months	18 months	24 months
RV1	4	1,559	337	169	112	0
	5	1,559	926	631	484	8
	6	1,559	167	93	64	0
Placebo	4	1,553	313	154	96	0
	5	1,553	862	578	455	7
	6	1,553	190	102	67	0

eFigure 9. Cumulative incidence of severe rotavirus gastroenteritis by length of interval between doses (4 weeks vs. 5 weeks vs. 6 weeks) in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



Vaccine Type	Number of doses $\geq 10$ weeks of age	N				
		12 weeks	6 months	12 months	18 months	24 months
RV5	Zero	1,030	2	0	0	0
	One	3,666	397	351	200	2
	Two	3,271	2,432	2,152	1,559	63
	Three	784	765	640	556	46
Placebo	Zero	1,029	6	2	0	0
	One	3,675	405	340	208	0
	Two	3,279	2,434	2,140	1,532	74
	Three	780	751	621	535	40

eFigure 10. Cumulative incidence of severe rotavirus gastroenteritis by number of doses received  $\geq 10$  weeks age (zero vs. one vs. two vs. three) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.

First dose with 4 – 6 weeks  
between doses

3 - 6 vs. 10 - 12 weeks

7 - 9 vs. 10 - 12 weeks

<sup>a</sup>

13 - 16 vs. 10 - 12 weeks

First dose

< 6 vs. ≥ 6 weeks

< 10 vs. ≥ 10 weeks

Last dose

≤ 15 vs. > 15 weeks

≤ 15 vs. > 15 weeks

Interval between doses

Both 4 vs. ≥ 1 of 6 weeks

≥ 1 of 5 weeks vs. ≥ 1 of 6 weeks

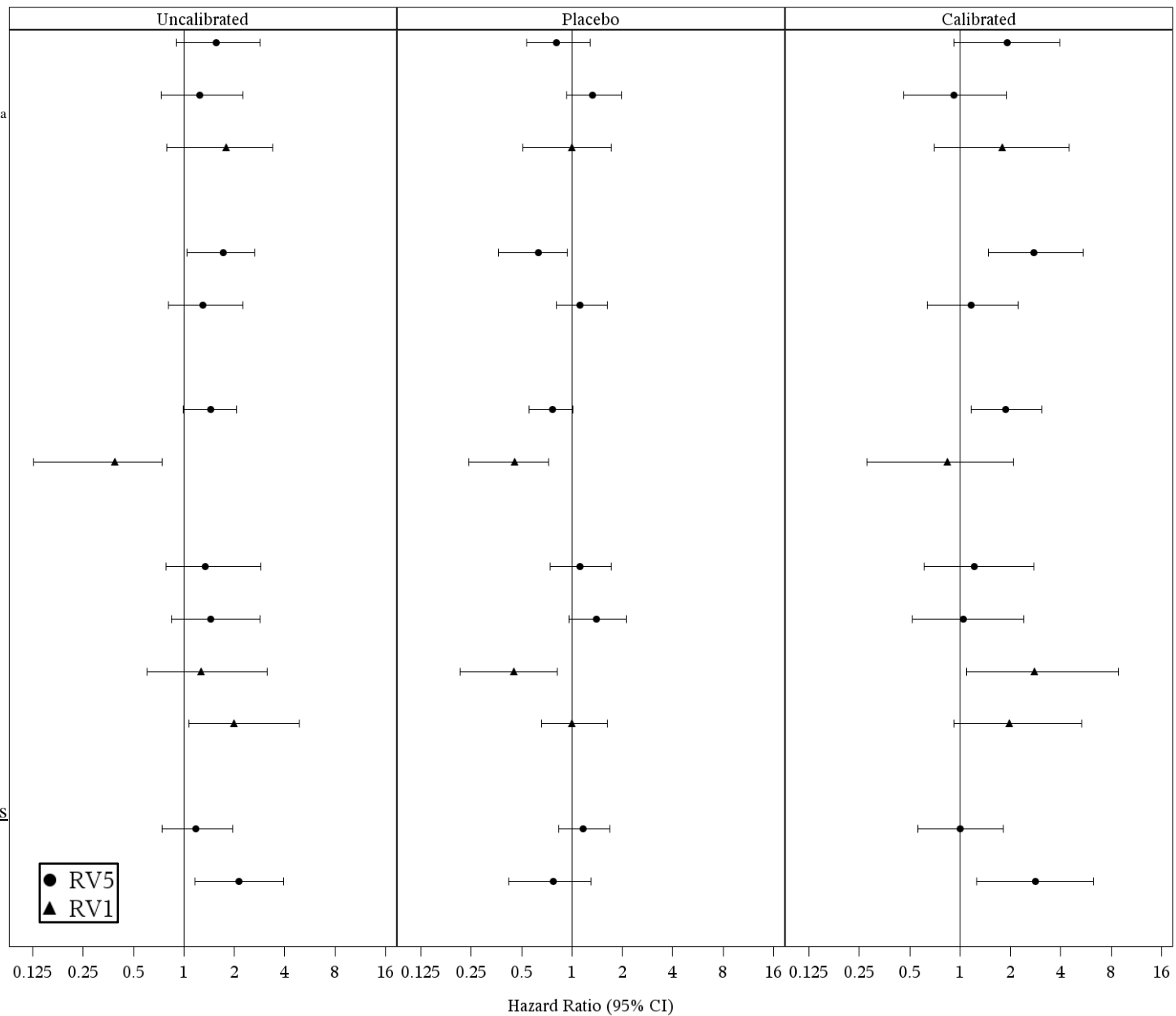
4 vs. 6 weeks

5 vs. 6 weeks

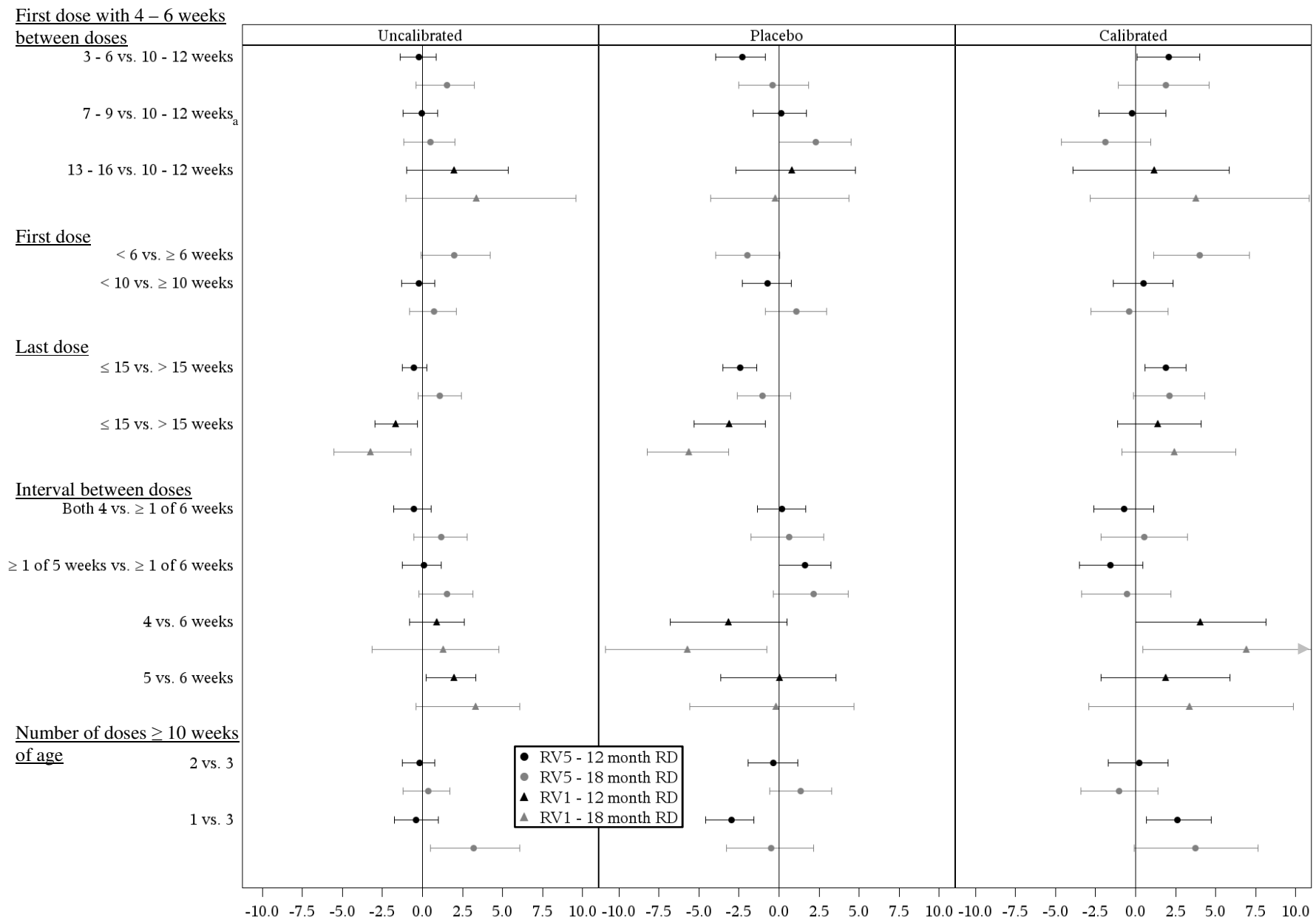
Number of doses ≥ 10 weeks  
of age

2 vs. 3

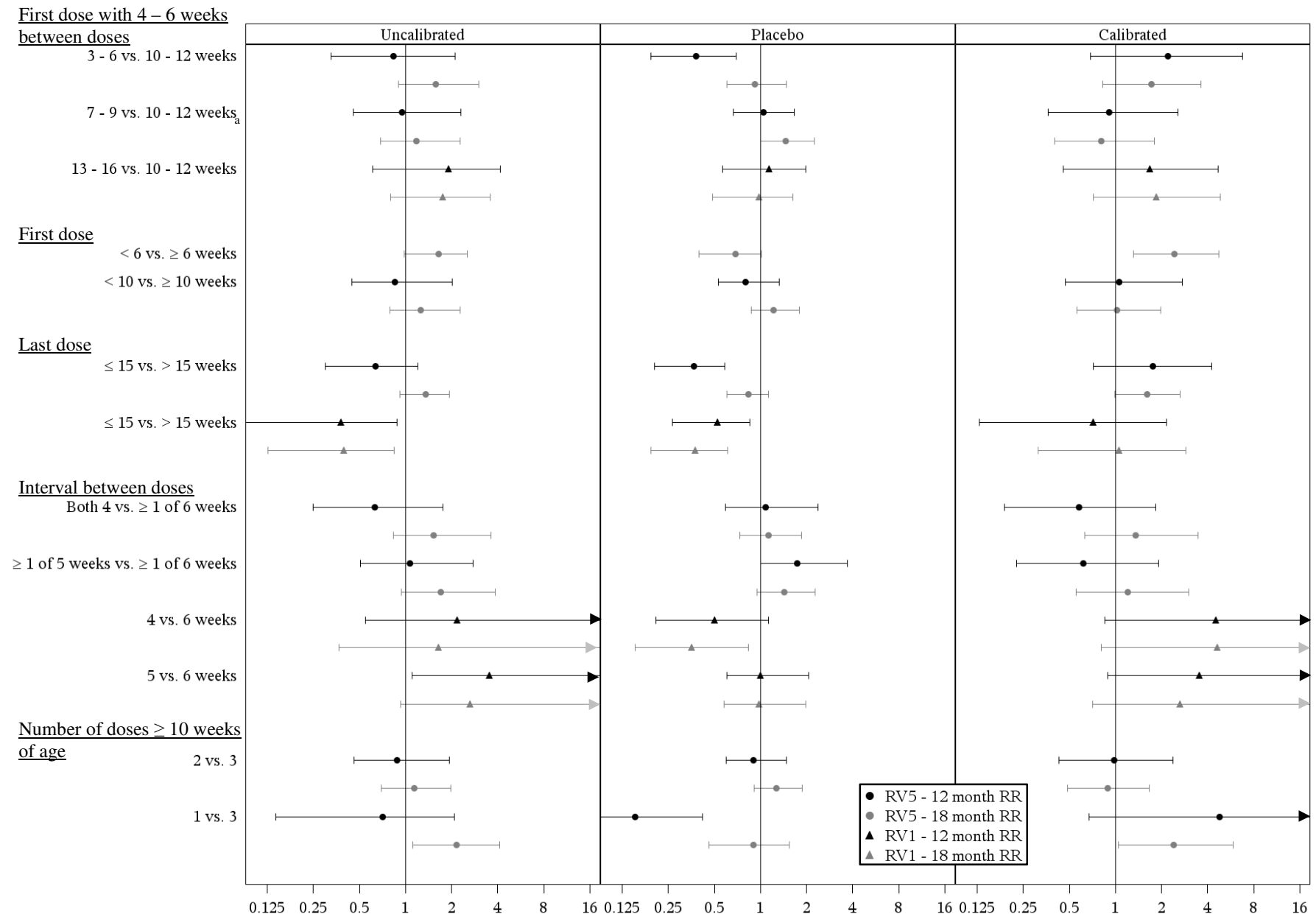
1 vs. 3



eFigure 11. Uncalibrated, placebo arm, and calibrated hazard ratios.



eFigure 12. Uncalibrated, placebo group, and calibrated risk differences.



eFigure 13. Uncalibrated, placebo group, and calibrated risk ratios.